DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Los Angeles District 9515d

19701 Fairchild
Irvine, California 92612-2506
Telephone (949) 608-2900

WARNING LETTER

CERTIFIED MAIL
RETURNED RECEIPT REQUESTED

December 22, 2004 W/L 06-05

David W. Powell
Worldwide President
Advanced Sterilization Products
33 Technology Drive
Irvine, CA 92618-2346

Dear Mr. Powell:

During an inspection of your medical device firm located in Irvine, California, from August 5, 2004 to October 4, 2004, our investigators determined that your firm manufactures and distributes the STERRAD® 50, STERRAD® 100 and STERRAD® 200 Sterilization Systems, the STERRAD® CycleSure™ Biological Indicators (BI), the Automatic Endoscope Reprocessor (AER), CIDEX® OPA Solution, CIDEX Plus 28 Day Solution and CIDEX® Activated Dialdehyde Solution. You also distribute the CIDEX® OPA Solution Test Strips and CIDEX® Activated Dialdehyde Solution Test Strips. The STERRAD® 50, STERRAD® 100 and STERRAD® 200 Sterilization Systems are intended to terminally sterilize medical devices, while the STERRAD® CycleSure™ Biological Indicators (BI) is intended to provide evidence that proper sterilization conditions are achieved in STERRAD® Systems. The Automatic Endoscope Reprocessor (AER) is intended to clean and disinfect endoscopes and the CIDEX® OPA Solution is used as the disinfectant. CIDEX® OPA Solution Test Strips are intended to determine whether the concentration of glutaraldehyde, the activated ingredient in CIDEX® Activated Dialdehyde Solution or CIDEX® OPA Solution, is above or below the minimum concentration (MEC) established for CIDEX® Activated Dialdehyde Solution or CIDEX® OPA Solution. The CIDEX® OPA Solution, CIDEX Plus 28 Day Solution and CIDEX® Activated Dialdehyde Solution are used as disinfectants. These products are devices as defined by Section 201 (h) of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C. § 321(h)].

Our inspection disclosed that the devices are adulterated within the meaning of Section 501(h) of the Act, 21 U.S.C. § 351(h), in that the methods used in, or the facilities or controls used for manufacturing, packing, storage, or installation are not in conformance with the Good Manufacturing Practice (GMP) requirements for the Quality System

Regulation, specified in Title 21, Code of Federal Regulations (CFR), Part 820, as follows:

1. Management with executive responsibility has not ensured an adequate and effective quality system has been fully implemented and maintained at all levels of the organization, as required by 21 CFR § 820.20. For example, your procedure that was in place in 2003, document number UP-01001 "Management Responsibility (Revision G)", issued 3/24/03, specifies that quarterly Management Reviews are to be conducted to review the overall quality system. We found one Management Review conducted on 8/1/03 but it was dated with signatures obtained on 8/30/04, 8/31/04 and 9/1/04.

2. Quality audits did not verify that the quality system is effective in fulfilling your quality system objectives, as required by 21 CFR § 820.22.

3. Failure to document corrective and preventive actions including the verification or validation of corrective actions, and the actions needed to correct or prevent recurrence of nonconforming product and other quality problems, as required by 21 CFR § 820.100(b). For example, CAPA #03-38 did not include an investigation for the assembly and post release processes of the CycleSure Biological Indicator (BI). The CAPA investigation only covered the contract manufacturing sites for the manufacturing of the ampoule and the Biological Indicator assembly site.

4. Failure to analyze and identify existing and potential causes of nonconforming product and other quality problems, as required by 21 CFR § 820.100(a)(1). For example, the number of allergic reactions related to CIDEX® OPA Solution complaints and the number of complaints resulting in MDRs reported in CAPA 02-066 dated 1/29/04 "Investigation Report: Allergic Reactions Associated with CIDEX® OPA Solution" is not consistent with the MDR log "January 2000 to present" and the list of "Allergic Reactions and Anaphylactic Complaints for CIDEX OPA-Updated 8/27/04".

5. Failure to define complaint handling procedures to ensure that all complaints are evaluated to determine whether the complaints should be filed as a Medical Device Report, as required by 21 CFR § 820.198(a)(3). Specifically, your procedure "Processing Complaints," document number SP-14042 (Revision B) issue date 8/16/04, does not require the investigation of technical service complaints.

6. Failure to evaluate and investigate complaints involving the possible failure of a device to meet its specifications, as required by 21 CFR § 820.198(c). Specifically, no investigation was documented for complaints #HD0402170063, #HD0312080078, HD0308210090, #HD0307150029, and #HD0306050067. Furthermore, the investigation of complaint #HD0407220040 is incomplete.

7. Failure to submit annually updated baseline reports, on the anniversary month of the initial submission, after the initial baseline report was submitted, as required by 21 CFR § 803.55(b). For example, changes in the manufacturing sites occurred after the initial baseline report was submitted on 3/23/00, but baseline reports were not updated until 8/20/04 for CIDEX® Activated Dialdehye Solution, CIDEX Plus 28 Day Solution and CIDEX® OPA Solution.

8. Failure to perform adequate validation of the device software, as required by 21 CFR § 820.30(g). For example, STERRAD® 200 sterilizer software version 2.0 lacks the identity and/or date of the person who performed the validation or a validation step was not completed. In addition, we found no raw data available for software changes made to the STERRAD® 50, STERRAD® 100 and STERRAD® 200 systems.

9. Failure to verify the device design confirms that the design output meets the design input requirements, as required by 21 CFR § 820.30(f). For example, your shelf-life for the CycleSure™ Biological Indicator Stability of the Bst SCBI is report RPT 1608-A dated 11/12/98. This document did not have charts/strips documenting temperature control parameters in the Device History Files for spore crops lot [redacted] and # [redacted] Furthermore, spore crop lot # [redacted] was replaced with lot [redacted] You state the replacement was due to a new formulation but we found no investigation of why lot # [redacted] at [redacted] month stability reported low D-values.

10. Failure to validate computer software for its intended use according to an established protocol, when computers or automated data processing systems are used as part of the quality system, as required by 21 CFR § 820.70(i). For example, you have no validation protocol for the complaint handling software.

We acknowledge receipt of your letters dated October 25, 2004, November 8 and 15, 2004, and December 2, 2004 in which you responded to the observations delineated on the form FDA 483 issued to you on October 4, 2004. Although some corrective actions have been implemented and appear to be adequate (i.e., your responses to Observations 2, 4a, 4e, 4f, 6, 7, 10, 11b, 11c, 12, 14, 15d, 15f, 15h, 15i, 15j, 17, 19, 20a, and 21 through 28), other responses are inadequate in a number of respects and thus do not address all of our concerns. We are prepared to discuss these concerns separately at a later time if you desire because of the proprietary information.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the Form FDA 483 issued at the conclusion of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance system. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

Federal Agencies are advised of the issuance of all Warning Letters pertaining to medical devices so that they may take this information into account when considering the award of contracts. Additionally, no premarket submissions for devices to which the GMP deficiencies are reasonably related will be cleared until the violations have been corrected. Also, no requests for Certificates For Exportability will be approved until the violations related to the subject devices have been corrected.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties.

You should notify this office within fifteen (15) working days of receipt of this letter of the specific steps you have taken to correct the noted violations including, an explanation of each step being taken to identify and prevent the recurrence of similar violations. If corrective action cannot be completed within (15) working days, state the reason for the delay and the time within which the corrections will be completed.

If you have any questions regarding this letter, please contact Ms. Mariza M. Jafary, Compliance Officer at 949-608-2977.

Your written reply should be addressed to:

Pamela Schweikert
Director, Compliance Branch
Food and Drug Administration
19701 Fairchild
Irvine, CA 92612-2446

Sincerely,

Alonza E. Cruse
District Director

Cc: State Department of Public Health
Environmental Health Services
Attn: Chief Food and Drug Branch
601 North 7th Street, MS-35
Sacramento, CA 94234-7320